

Med-Tox Group

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June 25, 2002

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket 01N-0322

Dear FDA:

Among ethical sponsors of clinical research, further need to assure ethics is probably unnecessary.

However, there are a growing number of unethical clinical research sponsors.

For example, ephedra alkaloid food supplement marketers systematically and intentionally violate IRB protections, the Declarations of Helsinki and the Nuremberg Code.

For example, ephedra marketers:

- a. Misrepresent the safety of their products to IRBs
- b. Although their products are based on drugs, comprised of drugs, marketed as drugs and researched as drugs, they falsely inform IRBs that FDA does not regulate their products, and their ephedra studies are immune from IND requirements...even though they have legal opinion that INDs are required (e.g., from the National Association for College and University Attorneys)
- c. Fail to notify IRBs the true safety hazards of products tested, the toxicity found in preclinical studies they sponsor, and that journal reviewers have determined submitted manuscripts about ephedra clinical research as reckless, baseless, and contradicting study results regarding safety claims
- d. Falsely represent safety of ephedra alkaloids added to the diet based on prescription drug studies of ephedrine/caffeine, while also failing to disclose

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study withdrawals in these drug studies due to clinically significant adverse reactions

- e. Support the testing of compounded unapproved new drugs (e.g., ephedrine? caffeine and aspirin; ephedrine/caffeine products have been banned in the US since 1983)
- f. Promote their products to treat diseases, and conduct associated clinical research. Ephedra disease claims are drug claims, and not approved by FDA or allowed by law (including the FDCA as amended by DSHEA)
- g. Within the protocol, specify an ephedra product for testing that is sufficiently illegal that the manufacturer is serving a 22-month prison sentence
- h. Fail to notify IRBs that their products contain a Schedule IV controlled substance and several known drugs; in some states, ephedra and ephedrine are controlled substances, facts also censored from IRBs
- i. Fail to notify IRBs of poor manufacturing and product adulteration; notably, in a leading research publication a year ago regarding ephedra, the placebo treatments were adulterated with at least two of the test drugs
- j. Violate protocol specifications and research ethics, and break treatment codes early in the study to post falsified press releases about study results
- k. Deny virtually everything known about ephedra alkaloid clinical pharmacology and toxicology
- l. Adulterate the placebo treatments with the test drugs
- m. Transfer at least one clinical trial to another university hospital after the initial one rejected its performance due to the IND requirement and added a warning about myocardial infarction to the Informed Consent form. This was a clear example of IRB shopping and misinformation.**

Having read a couple dozen depositions of the executives of ephedra businesses as well as hundreds of thousands of pages of litigation discovery documents, and having testified at trial and in several depositions about ephedra marketer fraud, negligence and IRB deceit, I have concluded that IRBs are primed for a collision, and inevitably will be sued by plaintiffs damaged by the IRB approvals based on falsified information.

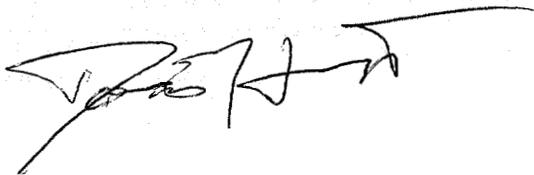
A problem more serious than already has occurred many times in ephedra clinical studies (e.g., study withdrawals for ephedra-induced chest pain, arrhythmia, hypertension) may prompt a larger media frenzy than occurred last year surrounding the Johns Hopkins debacle. Clinical research at major universities may also be shut down in the future over this fraudulent clinical research.

Egregiously, ephedra marketers are entirely unqualified to adequately formulate clinical research supplies, assemble product safety packages, monitor and analyze clinical research data, monitor and analyze tens of thousands of adverse event reports received, comply with relevant laws and regulations, and accurately present product safety to IRBs. Accordingly, IRB reliance on information from these clinical research sponsors is seriously flawed.

Ephedra products as well as dietary supplements clinical research is not immune to FDA, IND and IRB regulations, or to compliance with the Declarations of Helsinki and the Nuremburg Code.

At least regarding ephedra and dietary supplement clinical research, there must be additional safeguards to human subject protection.

Sincerely,

A handwritten signature in black ink, appearing to be 'J. H. H.', with a long horizontal line extending to the right.

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